

## **WHAT IS CLAIMED IS:**

1. A method of creating a chemical compound library comprising:  
selecting compounds having a molecular weight of no greater  
5 than about 350 grams/mole; and  
selecting compounds having a solubility in deuterated water of at  
least about 1 mM at room temperature.
2. The method of claim 1 wherein a majority of the compounds in the  
10 chemical compound library have a molecular weight of no greater than  
about 350 grams/mole and a solubility in deuterated water of at least  
about 1 mM at room temperature.
3. The method of claim 2 wherein all of the compounds in the chemical  
15 compound library have a molecular weight of no greater than about 350  
grams/mole and a solubility in deuterated water of at least about 1 mM at  
room temperature.
4. The method of claim 1 wherein the compounds selected have a molecular  
20 weight of no greater than about 325 grams/mole.
5. The method of claim 4 wherein the compounds selected have a molecular  
weight of less than about 325 grams/mole.
- 25 6. A chemical compound library comprising compounds having a molecular  
weight of no greater than about 350 grams/mole and a solubility in  
deuterated water of at least about 1 mM at room temperature.
7. The library of claim 6 wherein a majority of the compounds have a  
30 molecular weight of no greater than about 350 grams/mole and a  
solubility in deuterated water of at least about 1 mM at room  
temperature.
8. The library of claim 7 wherein all of the compounds have a molecular

weight of no greater than about 350 grams/mole and a solubility in deuterated water of at least about 1 mM at room temperature.

9. The library of claim 6 wherein the compounds have a molecular weight  
5 of no greater than about 325 grams/mole.
10. The library of claim 9 wherein the compounds have a molecular weight of less than about 325 grams/mole.
- 10 11. A method of identifying a lead chemical template, the method comprising:  
selecting compounds having a molecular weight of no greater than about 350 grams/mole and a solubility in deuterated water of at least about 1 mM at room temperature to create a chemical compound library;  
15 identifying at least one compound from the library that functions as a ligand to a target molecule having a dissociation constant of at least about 100  $\mu$ M; and  
using the ligand to identify a lead chemical template.
- 20 12. The method of claim 11 wherein a majority of the compounds in the chemical compound library have a molecular weight of no greater than about 350 grams/mole and a solubility in deuterated water of at least about 1 mM at room temperature.
- 25 13. The method of claim 12 wherein all of the compounds in the chemical compound library have a molecular weight of no greater than about 350 grams/mole and a solubility in deuterated water of at least about 1 mM at room temperature.
- 30 14. The method of claim 11 wherein the compounds selected for the library have a molecular weight of no greater than about 325 grams/mole.
15. The method of claim 14 wherein the compounds selected for the library

have a molecular weight of less than about 325 grams/mole.

16. The method of claim 11 wherein the dissociation constant of a lead chemical template to the target molecule is at least about 1  $\mu$ M.
- 5
17. The method of claim 11 wherein the target molecule is a protein.
18. A method of identifying a compound that binds to a target molecule, the method comprising:
- 10           providing a plurality of mixtures of test compounds, each mixture being in a sample reservoir;
- introducing a target molecule into each of the sample reservoirs to provide a plurality of test samples;
- providing a nuclear magnetic resonance spectrometer equipped
- 15           with a flow-injection probe;
- transferring each test sample from the sample reservoir into the flow-injection probe;
- collecting a relaxation-edited nuclear magnetic resonance spectrum on each sample in each reservoir; and
- 20           comparing the spectra of each sample to the spectra taken under the same conditions in the absence of the target molecule to identify compounds that bind to the target molecule;
- wherein the concentration of target molecule and each compound in each sample is no greater than about 100  $\mu$ M.
- 25
19. The method of claim 18 wherein each mixture is in a sample reservoir of a multiwell sample holder.
20. The method of claim 19 wherein the multiwell sample holder is a 96-well
- 30           microtiter plate.
21. The method of claim 18 wherein each test compound has a solubility in deuterated water of at least about 1 mM at room temperature.

22. The method of claim 18 wherein each test compound has a molecular weight of no greater than about 350 grams/mole.
- 5 23. The method of claim 18 wherein collecting a relaxation-edited nuclear magnetic resonance spectrum comprises collecting a 1D relaxation-edited nuclear magnetic resonance spectrum.
24. The method of claim 23 wherein collecting a 1D relaxation-edited  
10 nuclear magnetic resonance spectrum comprises collecting a 1D relaxation-edited  $^1\text{H}$  nuclear magnetic resonance spectrum.
25. The method of claim 18 wherein the mixture of compounds comprises at least about 3 compounds, each having at least one distinguishable  
15 resonance in a 1D NMR spectrum of the mixture.
26. The method of claim 25 wherein the mixture of compounds comprises at least about 6 compounds.
- 20 27. The method of claim 25 wherein the ratio of target molecule to each test compound in each sample reservoir is about 1:1.
28. The method of claim 18 wherein the concentration of target molecule and each compound in each sample is no greater than about 50  $\mu\text{M}$ .  
25
29. The method of claim 18 wherein the dissociation constant of a compound that binds to the target molecule is at least about 100  $\mu\text{M}$ .
30. The method of claim 18 wherein the target molecule is a protein.  
30
31. A method of identifying a compound that binds to a target molecule, the method comprising:  
providing a plurality of mixtures of test compounds, each mixture being in a sample reservoir;

introducing a target molecule into each of the sample reservoirs to provide a plurality of test samples;

providing a nuclear magnetic resonance spectrometer equipped with a flow-injection probe;

5           transferring each test sample from the sample reservoir into the flow-injection probe;

collecting a WaterLOGSY nuclear magnetic resonance spectrum on each sample in each reservoir; and

10           analyzing the spectra of each sample to distinguish binding compounds from nonbinding compounds by virtue of the opposite sign of their water-ligand NOEs.

32.   The method of claim 31 wherein the concentration of target molecule is no greater than about 10  $\mu$ M.

15

33.   The method of claim 32 wherein the concentration of target molecule is no greater than about 1  $\mu$ M.

20   34.   The method of claim 31 wherein the concentration of each compound in each sample is no greater than about 100  $\mu$ M.

35.   The method of claim 31 wherein each test compound has a solubility in deuterated water of at least about 1 mM at room temperature.

25   36.   The method of claim 31 wherein each mixture is in a sample reservoir of a multiwell sample holder.

37.   The method of claim 36 wherein the multiwell sample holder is a 96-well microtiter plate.

30

38.   The method of claim 31 wherein each test compound has a molecular weight of no greater than about 350 grams/mole.

39. The method of claim 38 wherein each test compound has a molecular weight of no greater than about 325 grams/mole.
40. The method of claim 31 wherein collecting a WaterLOGSY nuclear magnetic resonance spectrum comprises collecting a 1D WaterLOGSY nuclear magnetic resonance spectrum.
41. The method of claim 31 wherein the mixture of compounds comprises at least about 3 compounds, each having at least one distinguishable resonance in a 1D NMR spectrum of the mixture.
42. The method of claim 41 wherein the mixture of compounds comprises at least about 6 compounds.
43. The method of claim 31 wherein the ratio of target molecule to each test compound in each sample reservoir is about 100:1 to about 10:1.
44. The method of claim 31 wherein the dissociation constant of a compound that binds to the target molecule is at least about 100  $\mu\text{M}$ .
45. The method of claim 31 wherein the target molecule is a protein.